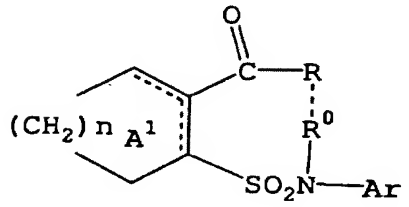
AMENDMENTS TO THE CLAIMS

Listing of Claims:

1-4. (Cancelled).

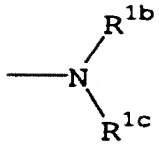
5. (Currently Amended) A method for the ~~prophylaxis or~~ treatment of severe sepsis associated with organ failure, hypoperfusion and/or hypotension, which comprises administration of an effective amount of a compound represented by the formula (I):~~or the formula (II) or a salt thereof or a prodrug thereof described in claim 2 to a mammal.~~



(I)

wherein

R represents an aliphatic hydrocarbon group optionally having substituents, an aromatic hydrocarbon group optionally having substituents, a heterocyclic group optionally having substituents, a group represented by the formula: $-OR^1$ wherein R^1 represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents, or a group represented by the formula:



wherein

R^{1b} and R^{1c}

are the same or different and each represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents,

R^O represents a hydrogen atom or an aliphatic hydrocarbon group, or R and R^O in combination form a bond,

ring A^1 represents a cycloalkene optionally substituted by 1 to 4 substituents selected from the group consisting of

(1) an aliphatic hydrocarbon group optionally having substituents,

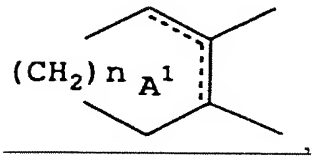
(2) an aromatic hydrocarbon group optionally having substituents,

(3) a group represented by the formula: $-OR^{11}$ wherein R^{11} represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents and

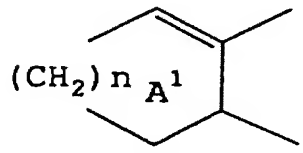
(4) a halogen atom,

Ar represents an aromatic hydrocarbon group optionally having substituents,

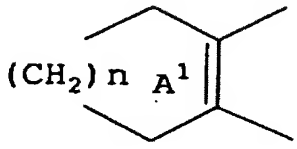
a group represented by the formula:



or a group represented by the formula:



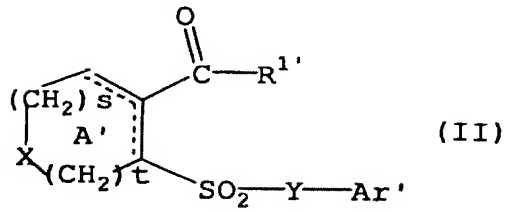
or



, and

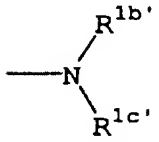
wherein n represents an integer of 1 to 4,

or a salt thereof, or a compound represented by the formula (II):



(II)

wherein $R^{1'}$ represents an aliphatic hydrocarbon group optionally having substituents, an aromatic hydrocarbon group optionally having substituents, a heterocyclic group optionally having substituents, a group represented by the formula: $-OR^{1a'}$ wherein $R^{1a'}$ represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents, or a group represented by the formula:



(a)

wherein $R^{1b'}$ and $R^{1c'}$ are the same or different and each represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents,

X represents a methylene group, NH, a sulfur atom or an oxygen atom,

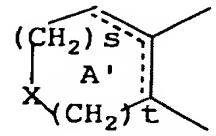
Y represents a methylene group optionally having substituents or NH optionally having substituents,

ring A' represents a 5- to 8-membered ring optionally having 1 to 4 substituents selected from the group consisting of (1) an aliphatic hydrocarbon group optionally having substituents, (2) an aromatic hydrocarbon group optionally having

substituents, (3) a group represented by the formula: $-OR^{2'}$ wherein $R^{2'}$ represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents and (4) a halogen atom,

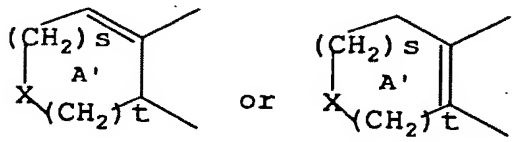
Ar' represents an aromatic hydrocarbon group optionally having substituents,

a group represented by the formula:



(b)

represents a group represented by the formula:



(b1) or (b2)

s represents an integer of 0 to 2,

t represents an integer of 1 to 3, and

the total of s and t is not more than 4;

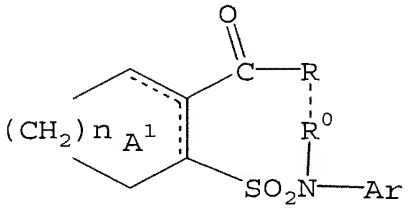
provided that when X is a methylene group, Y represents a methylene group optionally having substituents, or a salt thereof ~~the formula (I) or the formula (II) or a salt thereof or a prodrug thereof described in claim 2~~ to a mammal.

6. (Cancelled).

7. (Withdrawn) A TLR signal inhibitor comprising a non-peptide compound as an active ingredient.

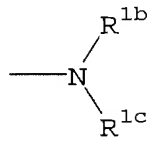
8. (Withdrawn) The agent of claim 7, wherein the non-peptide compound is a non-peptide compound having a molecular weight of not more than about 1000.

9. (Withdrawn) The agent of claim 8, wherein the non-peptide compound is a compound represented by the formula (I):



(I)

wherein R represents an aliphatic hydrocarbon group optionally having substituents, an aromatic hydrocarbon group optionally having substituents, a heterocyclic group optionally having substituents, a group represented by the formula: $-OR^1$ wherein R^1 represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents, or a group represented by the formula:



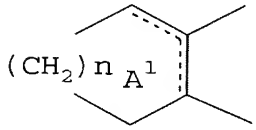
wherein R^{1b} and R^{1c} are the same or different and each represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents,

R^0 represents a hydrogen atom or an aliphatic hydrocarbon group, or R and R^0 in combination form a bond,

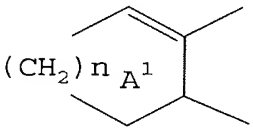
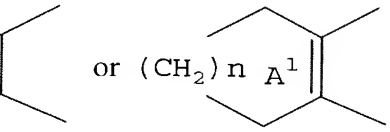
ring A^1 represents a cycloalkene optionally substituted by 1 to 4 substituents selected from the group consisting of (1) an aliphatic hydrocarbon group optionally having substituents, (2) an aromatic hydrocarbon group optionally having substituents, (3) a group represented by the formula: $-OR^{11}$ wherein R^{11} represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents and (4) a halogen atom,

Ar represents an aromatic hydrocarbon group optionally having substituents,

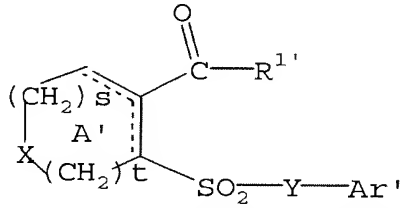
a group represented by the formula:



represents a group represented by the formula:

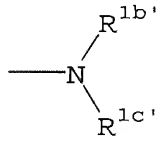
 or  , and

n represents an integer of 1 to 4, or a salt thereof or a prodrug thereof, or, a compound represented by the formula (II):



(II)

wherein $R^{1'}$ represents an aliphatic hydrocarbon group optionally having substituents, an aromatic hydrocarbon group optionally having substituents, a heterocyclic group optionally having substituents, a group represented by the formula: $-OR^{1a'}$ wherein $R^{1a'}$ represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents, or a group represented by the formula:



(a)

wherein $R^{1b'}$ and $R^{1c'}$ are the same or different and each represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents,

X represents a methylene group, NH, sulfur atom or oxygen atom,

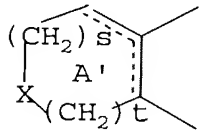
Y represents a methylene group optionally having substituents or NH optionally having substituents,

ring A' represents a 5 to 8-membered ring optionally having 1 to 4 substituents selected from the group consisting of (1) an aliphatic hydrocarbon group optionally having substituents, (2) an aromatic hydrocarbon group optionally having substituents, (3) a group represented by the

formula: -$OR^{2'}$ wherein $R^{2'}$ represents a hydrogen atom or an aliphatic hydrocarbon group optionally having substituents and (4) a halogen atom,

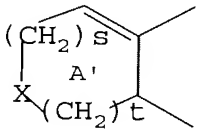
Ar' represents an aromatic hydrocarbon group optionally having substituents,

a group represented by the formula:

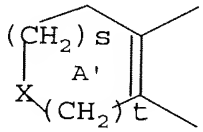


(b)

represents a group represented by the formula:



or



,

(b1) (b2)

s represents an integer of 0 to 2,

t represents an integer of 1 to 3,

the total of s and t is not more than 4;

provided that when X is a methylene group, Y represents a methylene group optionally having substituents, or a salt thereof or a prodrug thereof.

10. (Withdrawn) The agent of claim 7, wherein TLR is TLR4.

11. (Withdrawn) An agent for the prophylaxis or treatment of a disease caused by a change in a TLR signal, which comprises the agent of claim 7.

12. (Withdrawn) The agent of claim 11, wherein the disease caused by the changes in the TLR signal is organ dysfunction.

13. (Withdrawn) The agent of claim 12, wherein the organ is an organ of central nervous system, circulatory system, respiratory system, bone and joint system, digestive system or renal and urinary system.

14. (Withdrawn) A method for the inhibition of TLR signal, which comprises administration of an effective amount of a non-peptide compound to a mammal.

15. (Withdrawn) A method for the prophylaxis or treatment of a disease caused by a change in a TLR signal, which comprises administration of an effective amount of a non-peptide compound to a mammal.

16. (Withdrawn) Use of a non-peptide compound for the production of a TLR signal inhibitor.

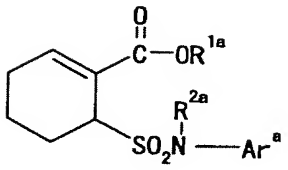
17. (Withdrawn) Use of a non-peptide compound for the production of an agent for the prophylaxis or treatment of a disease caused by a change in a TLR signal.

18. (Withdrawn) An agent for the prophylaxis or treatment of organ dysfunction, which comprises a TLR signal inhibitory substance.

19. (Withdrawn) The agent of claim 18, wherein the organ is an organ of central nervous system, circulatory system, respiratory system, bone and joint system, digestive system or renal and urinary system.

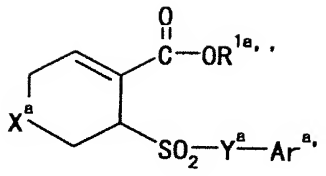
20. (Withdrawn) A method for the prophylaxis or treatment of severe sepsis or organ dysfunction, which comprises inhibition of TLR signal.

21. (New) The method of claim 5, wherein the formula (I) is the formula (Ia):



(Ia)

wherein R^{1a} represents a C_{1-6} alkyl, R^{2a} represents a hydrogen atom or a C_{1-6} alkyl and Ar^a represents a phenyl group substituted by 1 or 2 halogen atoms, and the formula (II) is the formula (IIa):



(IIa)

wherein $R^{1a''}$ represents a C_{1-6} alkyl, X^a represents a methylene group or an oxygen atom, Y^a represents a methylene group or -NH- and $Ar^{a'}$ represents a phenyl group optionally having 1 or 2 substituents selected from a halogen atom and a C_{1-6} alkoxy group, provided that when X^a is a methylene group, Y^a represents a methylene group.

22. (New) The method of claim 5, further comprising administration of an effective amount of at least one kind of drug selected from the group consisting of antibacterial agent, antifungal agent, non-steroidal antiflammatory drug, steroid and anticoagulant.

23. (New) The method of claim 5, wherein the compound is
d-ethyl 6-[N-(2,4-difluorophenyl) sulfamoyl]-1-cyclohexene-1-carboxylate,
ethyl 6-[N-(2-chlorophenyl) sulfamoyl]-1-cyclohexene-1-carboxylate,
ethyl 6-[N-(2-chloro-4-methylphenyl) sulfamoyl]-1-cyclohexene-1-carboxylate,
ethyl (6R)-6-[(2-chloro-4-fluoroanilino) sulfonyl]-1-cyclohexene-1-carboxylate, or a salt thereof; or
ethyl 6-[(2-chloro-4-fluorobenzyl) sulfonyl]-1-cyclohexene-1-carboxylate,
ethyl (+)-6-[(2-chloro-4-fluorobenzyl) sulfonyl]-1-cyclohexene-1-carboxylate,
ethyl 3-[(2-chloro-4-fluorophenyl) sulfamoyl]-3, 6-dihydro-2H-pyran-4-carboxylate, or a salt thereof.